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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,068	07/13/2006	Parry John Guilford	210.1USWO	3673

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
11/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,068	GUILFORD ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-30* is/are pending in the application.

4a) Of the above claim(s) *3-6,13-18 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 8-12, 19-21 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II (claims 1, 2, 8-12, 19-21 and 25-27) in the reply filed on July 30, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-30 are pending.

Claims 3-6, 13-18 and 22-24,

Claim 7 has been cancelled.

Claims 28-30 have been added.

Claims 1, 2, 8, 9, 19-21 and 27 have been amended.

Claims 1, 2, 8-12, 19-21 and 25-30 are examined on the merits.

Claim Objections

3. Claim 2 is objected to because of the following informalities: citation of italicized misspelled words in the two terms, *phosphlipase* A2 and transforming growth B induced *protin*. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 8-12, 19-21 and 25-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of detecting gastric cancer comprising detecting and measuring a cystatin SN or cystatin SN peptide in a biological sample. The specification does not adequately define the term, cystatin SN. Hence, the written description in this instant case has not been adequately defined. There is no SEQ ID number set forth in the claims which corresponds to the term which would aid in clearly establishing what Applicants are in possession, nor any characterization or description of cystatin SN. The written description is not commensurate in scope with the claims that embody the broad term, cystatin SN.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*. (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that

[he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the nucleic acid and the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed it is not clear what Applicants have possession in regard to the broadly termed cystatin SN. This term encompasses

variants and mutants and polypeptides that share less than 100% sequence identity with the wild-type cystatin SN equence. The specification does not evidence the possession of all the possible mutant polypeptides. There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims do not meet the written description provision of 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 2, 8-12, 19-21, 25-27, 29 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number US 2004/0076955 A1 (filed July 2, 2002). The publication discloses a method of diagnosing a colon, small intestine and large intestine disorder comprising identifying and comparing diagnostic markers listed in Tables 1A-13 including cystatin SN, see page 2, sections 0026-0030;

page 3, section 0054; page 11, section 0108; page 21, section 0209; page 108, Table 4a; and page 112, Table 6A, Pkey number 409757. The diagnostic markers are detected in biological samples include sections of tissues such as biopsy and autopsy samples, plasma, serum, stool, urine, and mucus, see page 4, sections 0059 and 0060. Diagnostic assays implemented include standard immunoassays, such as ELISAs using antibodies capable of detecting polypeptides and peptides, see page 4, section 0057; page 5, section 0069; page 21, section 0209; and page 22, section 0217. A number of markers are evaluated for differential expression between normal and cancerous tissues, see page 21, sections 0207-0209. Examples of additional diagnostic markers to be assessed are olfactomedin (page 35); SPARC-like 1 (page 36); matrix metalloproteinase 12, inhibin (pages 45, 55 and 58); lysyl oxidase (page 54); lumican (page 126); thrombospondin 2 (page 134); TGFB inducible early growth response (page 9A); kallikrein 11 (page 150); aldican (page 154); and chondroitin sulfate proteoglycan 2 (page 167).

8. Claims 1, 19 and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Utsunomiya et al. (Clinical Cancer Research 8: 2591-2594, August 2002). Claims are given their broadest reasonable interpretation. Consequently, in absence of a definition or characterization of cystatin SN the prior art is applicable. Utsunomiya discloses a method of detecting the expression of cystatin-like metastasis-associated protein (CMAP) in colorectal tumor tissue specimens, see abstract; and page 2592, 1st paragraph and Table 1.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 2, 8-12, 19-21 and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication number US 2004/0076955 A1 (filed July 2, 2002), and further in view of U.S. Patent Application Publication number US 2006/0019256 A1 (effective filing date June 9, 2003). The teachings of publication '76955 have been set forth in the preceding 102(e) rejection. This publication does not teach measuring overexpression of serine or cysteine proteinase inhibitor clade H (SERPINH1) and serine or cysteine proteinase inhibitor clade B (SERPINB5).

However, publication '19256 teaches characterizing and diagnosing cancer, for example colon carcinoma comprising identifying tumor cancer markers, such as SERPINB5 (page 12, line 24 from the bottom of the page) and SERPINH1 (page 13, line 16). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include these additional cancer markers. One of ordinary skill in the art would have been motivated to use these particular markers because the secondary reference teaches these markers' upregulated expression is consistent with solid tumors, such as colon carcinoma and breast cancer.

10. Claims 1, 2, 8-12, 19-21 and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03/057916 A2 (filed January 9, 2003), and further in view of U.S. Patent Application Publication number US 2004/0076955 A1 (filed July 2, 2002) and U.S. Patent Application Publication number US 2006/0019256 A1 (effective filing date June 9, 2003).

WO 03/057916 teaches a method of detecting the level of expression of cancer markers in biological samples, including plasma, fluids and the like by immunohistochemistry methods to diagnose a cancer, see page 6, lines 3-19; page 24, lines 4-11; and page 28, lines 15-24. The expression profiles of a number of xenografts including colon samples were established, see page 6, lines 3-19; and page 61, Example 2. The WO document does not teach the specific gastric tumor markers listed in claims 1 and 2.

However, U.S. Patent Application Publication number US 2004/0076955 A1 (filed July 2, 2002) teaches a method of diagnosing a colon, small intestine and large intestine disorder comprising identifying and comparing diagnostic markers listed in Tables 1A-13 including cystatin SN, see page 2, sections 0026-0030; page 3, section 0054; page 11, section 0108; page 21, section 0209; page 108, Table 4a; and page 112, Table 6A, Pkey number 409757. The diagnostic markers are detected in biological samples include sections of tissues such as biopsy and autopsy samples, plasma, serum, stool, urine, and mucus, see page 4, sections 0059 and 0060. Diagnostic assays implemented include standard immunoassays, such as ELISAs using antibodies capable of detecting polypeptides and peptides, see page 4, section 0057; page 5,

section 0069; page 21, section 0209; and page 22, section 0217. A number of markers are evaluated for differential expression between normal and cancerous tissues, see page 21, sections 0207-0209. Examples of additional diagnostic markers to be assessed are olfactomedin (page 35); SPARC-like 1 (page 36); matrix metalloproteinase 12, inhibin (pages 45, 55 and 58); lysyl oxidase (page 54); lumican (page 126); thrombospondin 2 (page 134); TGFB inducible early growth response (page 9A); kallikrein 11 (page 150); aldican (page 154); and chondroitin sulfate proteoglycan 2 (page 167). U.S. Patent Application Publication number US 2006/0019256 A1 (effective filing date June 9, 2003) teaches characterizing and diagnosing cancer by assessing several markers, serine or cysteine proteinase inhibitor clade B (SERPINB5), secreted acidic cysteine-rich protein (SPARC) see page 12, lines 2 and the 25th line from the bottom of the page and serine or cysteine proteinase inhibitor clade H (SERPINH1), see page 13, line 16. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include these cancer markers for gastric cancer diagnosis. One of ordinary skill in the art would have been motivated to use these particular markers because the secondary references teach these markers' upregulated expression is consistent with solid tumors, such as colon carcinoma and breast cancer.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be

reached between the hours of 7:30 am to 6:30 pm, Monday-Saturday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
6 November 2008
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643